SUPPLEMENTAL AMENDMENT AND RESPONSE UNDER 37 CFR § 1.116 – EXPEDITED PROCEDURE

Serial Number: 10/722,115

Filing Date: November 25, 2003

Title: METHOD AND APPARATUS FOR CELL AND ELECTRICAL THERAPY OF LIVING TISSUE

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IN THE CLAIMS

Please amend the claims as follows:

1. (Currently Amended) An apparatus adapted for *in vitro* conditioning of cells prior to a cell therapy, the apparatus comprising:

a culturing module to host the cells and a culturing medium;

a cardiac electrical stimulator coupled to the culturing module and adapted to create cardiac electrical conditions in the culturing medium by delivering electrical stimuli, the cardiac electrical conditions simulating electrical conditions in the myocardium that result in cardiac contraction;

a myocardial stress simulator coupled to the culturing module and adapted to create a mechanical stress upon the cells by delivering mechanical stimuli, the mechanical stress simulating a tension applied upon cardiac muscle cells in the myocardium;

a biological treatment administration module coupled to the culturing module and adapted to deliver biological stimuli <u>including one or more biological agents selected from</u> protein and nucleic acid;

a memory circuit including an instruction set adapted to condition for an automatic process of conditioning the cells for administration into tissue of myocardium, the instruction set defining a predetermined sequence of one or more the electrical stimuli, the mechanical stimuli, and the biological stimuli; and

a controller coupled to the cardiac electrical stimulator, the myocardial stress simulator, the biological treatment administration module, and the memory circuit, the controller adapted to control the cardiac electrical stimulator, the myocardial stress simulator, and the biological treatment administration module by automatically executing the instruction set.

2. (Original) The apparatus of claim 1, further comprising two or more electrodes, connected to the cardiac electrical stimulator and disposed in the culturing medium, to allow delivery of at least one electrical stimulus to the cells.

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3. (Original) The apparatus of claim 2, wherein the electrical stimulator comprises a

pacemaker.

4. (Original) The apparatus of claim 3, wherein the cardiac electrical stimulator comprises an

electric field generator.

5. (Original) The apparatus of claim 1, wherein the culturing module comprises a deformable

culturing substrate allowing the cells to be plated thereon.

6. (Original) The apparatus of claim 5, wherein the deformable culturing substrate is made of

silicone.

7. (Original) The apparatus of claim 6, wherein the myocardial stress simulator comprises a

variable speed motor and a mechanical linkage coupled between the variable speed motor and

the deformable culturing substrate, the variable speed motor and the mechanical linkage adapted

to create a calibrated cyclic mechanical tension upon the deformable culturing substrate.

8. (Currently Amended) The apparatus of claim 1, wherein the biological treatment

administration module comprises one or more ehemical dispensers adapted to release $\underline{\text{the}}$ one or

more biological stimulation agents into the culturing medium.

9. (Original) The apparatus of claim 8, wherein the culturing module comprises a mixer

adapted to create and maintain a homogeneous culturing medium.

10. (Original) The apparatus of claim 1, further comprising a user interface coupled to the

controller, the user interface including a use input accepting commands.

11. (Canceled)

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- The apparatus of claim 10, wherein the user interface comprises a 12. (Previously Presented) display screen.
- 13. (Original) The apparatus of claim 12, further comprising a monitor coupled to the culturing module, the monitor adapted for observation of the cells in the culturing module.
- 14. (Original) The apparatus of claim 13, wherein the monitor comprises a microscope, coupled to the controller and the user interface, to allow observation of the cells on the display screen.
- 15-72. (Canceled)
- The apparatus of claim 1, wherein the controller is adapted to 73. (Previously Presented) allow adjustment of parameters in the instruction set during the in vitro conditioning of the cells.
- 74. (Previously Presented) The apparatus of claim 7, wherein the mechanical linkage is adapted to allow the culturing substrate to be stretched and relaxed in two or more directions without vibration and hesitation.
- The apparatus of claim 1, wherein the biological treatment 75. (Currently Amended) administration module comprises an array of dispensers each adapted [[for]] to release [[of]] a predetermined amount of the one or more of chemical and biological agents into the culturing medium.
- The apparatus of claim 3, wherein the controller is adapted to 76. (Previously Presented) control a pacing voltage and a pacing pulse width.
- The apparatus of claim 5, wherein the controller is adapted to 77. (Previously Presented) control a frequency and a degree of cell deformation.

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78. (Previously Presented) The apparatus of claim 8, wherein the controller is adapted to control a volume and a concentration of each of the one or more biological agents.

- 79. (Previously Presented) The apparatus of claim 14, wherein the controller is adapted to process an image of the cells and present the image on the display screen.
- 80. (New) The apparatus of claim 1, wherein the biological treatment administration module includes one or more isolated nucleic acid molecules whose expression in the cells enhances one or more of proliferation, engraftment, survival, and differentiation of the cells after their administration into the tissue of myocardium.
- 81. (New) The apparatus of claim 1, wherein the biological treatment administration module includes one or more of:
 - a differentiation factor;
 - a growth factor;
 - an angiogenic protein;
 - a survival factor;
 - a cytokine; and

isolated nucleic acid molecules encoding a gene product including one or more of an angiogenic protein, a growth factor, a differentiation factor, a survival factor, a cytokine, a cardiac cell-specific structural gene product, a cardiac cell-specific transcription factor, a membrane protein, and an antisense sequence.